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Attorney Docket No.: 6213.200-US PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Thomas-Hoeg-Jensen et al.

Serial No.: 09/870,884 Group Art Unit: 1646

Filed: May 31, 2001 Examiner: To be assigned

For: Glucose Dependent Release Of Insulin From Glucose Sensing Insulin Derivatives

RESPONSE TO NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCES AND/OR AMINO ACID SEQUENCE DISCLOSURES

Mail Stop Sequence
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This paper is submitted in response to the Notice to Comply mailed February 10, 2003 (a copy of which is attached hereto), having a two (2) month period for response due to expire April 10, 2003, with extensions of time available pursuant to 37 CFR §1.136(a). Applicant encloses herewith a Petition for Extension of Time for a period of four (4) months to permit timely filing of this response.

Please amend the above-identified application as follows:

In the Specification:

Please insert the following immediately after the sentence that ends on page 3, line 29 of the specification as filed:

-- The sequence of human insulin, A and B chains, is as follows:

Human insulin, A chain: G-I-V-E-Q-C-C-T-S-I-C-S-L-Y-Q-L-E-N-Y-C-N (SEQ ID NO: 1); Human insulin, B chain: F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-P-K-T (SEQ ID NO: 2). Analogs of human insulin exemplified in the instant invention include, but are not limited to the following: Human insulin, Asp^{B28} B chain analog: F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-D-K-T (SEQ ID NO: 3);

Human insulin, Lys^{B28}, Pro^{B29} B chain analog:

F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-K-P-T (SEQ ID NO: 4);

Human insulin, Gly^{A21} A chain analog:

G-I-V-E-Q-C-C-T-S-I-C-S-L-Y-Q-L-E-N-Y-C-G (SEQ ID NO: 5);

Human insulin, Lys^{B3}, Ile^{B28} B chain analog:

F-V-K-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-I-K-T (SEQ ID NO: 6);

Human insulin, Asp^{A21} A chain analog:

G-I-V-E-Q-C-C-T-S-I-C-S-L-Y-Q-L-E-N-Y-C-D (SEQ ID NO: 7);

Human insulin, des^{B30} B chain analog:

F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-P-K (SEQ ID NO: 8);

Human insulin, Phe^{B26} B chain analog:

F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-F-T-P-K-T (SEQ ID NO: 9);

Human insulin, Orn^{B30} B chain analog:

F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-P-K-X (SEQ ID NO: 10)

X = ornithine;

Human insulin, Dap^{B30} B chain analog:

F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-P-K-X (SEQ ID NO: 11)

X = diaminopropionic acid;

Human insulin, Lys^{B30} B chain analog:

F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-P-K-K (SEQ ID NO: 12);

Human insulin, Pro^{B0} B chain analog:

P-F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-P-K-T (SEQ ID NO: 13);

Human insulin, Asp^{B30} B chain analog:

F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-P-K-D (SEQ ID NO: 14);

Human insulin, Glu^{B30} B chain analog:

F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-P-K-E (SEQ ID NO: 15);

Human insulin, $Ams(BOC)^{B30}$ B chain analog:

F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-P-K-X (SEQ ID NO: 16)

X = O-aminoserine(BOC); and

Human insulin, Dab^{B30} B chain analog:

F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-P-K-X (SEQ ID NO: 17)

X = diaminobutyric acid. --

REMARKS

The specification has been amended to provide SEQ ID NOs for human insulin A and B chains referred to in the citation at page 3, lines 28-29 of the specification, as well as the human insulin analogs disclosed in the Examples section of the specification.

Applicant encloses herewith the Sequence Listing for the above-identified application and a 3.5" diskette containing a computer readable form of the Sequence Listing. Applicant respectfully requests entry of the Sequence Listing in the pending application.

In accordance with 37 CFR §1.821(f), I hereby state that the content of the paper and computer readable copies of the Sequence Listing is the same. No new matter has been added by entry of this amendment.

Attached hereto is a marked-up version of the changes made to the specification by the current amendment. The attached page is captioned "Version With Markings To Show Changes Made".

The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

Date: July 18, 2003

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Version With Markings To Show Changes Made

In the specification:

Paragraph beginning on page 3, line 24 has been amended as follows:

By "analogue of human insulin" as used herein (and related expressions) is meant human insulin in which one or more amino acid residues have been deleted and/or replaced by other amino acid residues, including non-codeable amino acid residues, or human insulin comprising additional amino acid residues, i.e. more than 51 in total. The amino acid sequence of human insulin is given *i.a.* in The Merck Index, 11th Edition, published in 1989 by Merck & Co., Inc., page 4888. The sequence of human insulin, A and B chains, is as follows: Human insulin, A chain: G-I-V-E-Q-C-C-T-S-I-C-S-L-Y-Q-L-E-N-Y-C-N (SEQ ID NO: 1); Human insulin, B chain: F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-P-K-T (SEQ ID NO: 2). Analogs of human insulin exemplified in the instant invention include, but are not limited to the following: Human insulin, Asp^{B28} B chain analog: F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-D-K-T (SEQ ID NO: 3); Human insulin, Lys^{B28}, Pro^{B29} B chain analog: F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-K-P-T (SEQ ID NO: 4); Human insulin, Gly^{A21} A chain analog: G-I-V-E-Q-C-C-T-S-I-C-S-L-Y-Q-L-E-N-Y-C-G (SEQ ID NO: 5); Human insulin, Lys^{B3}, Ile^{B28} B chain analog: F-V-K-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-I-K-T (SEQ ID NO: 6); Human insulin, Asp^{A21} A chain analog: G-I-V-E-Q-C-C-T-S-I-C-S-L-Y-Q-L-E-N-Y-C-D (SEQ ID NO: 7); Human insulin, des^{B30} B chain analog: F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-P-K (SEQ ID NO: 8); Human insulin, Phe^{B26} B chain analog: F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-F-T-P-K-T (SEQ ID NO: 9); Human insulin, Orn^{B30} B chain analog: F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-P-K-X (SEQ ID NO: 10)

X = ornithine;

Human insulin, Dap^{B30} B chain analog:

F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-P-K-X (SEQ ID NO: 11)

X = diaminopropionic acid;

Human insulin, Lys^{B30} B chain analog:

F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-P-K-K (SEQ ID NO: 12);

Human insulin, Pro^{B0} B chain analog:

P-F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-P-K-T (SEQ ID NO: 13);

Human insulin, Asp^{B30} B chain analog:

F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-P-K-D (SEQ ID NO: 14);

Human insulin, Glu^{B30} B chain analog:

F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-P-K-E (SEQ ID NO: 15);

Human insulin, $Ams(BOC)^{B30}$ B chain analog:

F-V-N-Q-H-L-C-G-S-H-L-V-E-A-L-Y-L-V-C-G-E-R-G-F-F-Y-T-P-K-X (SEQ ID NO: 16)

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X = diaminobutyric acid.